Implementation and Investigation of a Bone Adaptation Theory in MATLAB

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Abstract: **It is currently believed that trabecular architecture in bone is result of adaptation process in which mechanical loads play a dominant role. Huiskes et al (2000) proposed a regulatory mechanism for this process. We implemented this model in a MATLAB code and studied effect of changing different parameters and other capabilities of such a mechanism. Starting from different initial configurations and by changing loading magnitude and direction in a plate model, we observed that this model always produces trabecular-like structures similar to those produced in simulation series performed by Huiskes and co-workers. In addition to confirming results of earlier simulations, such a general computer code can provide us with a better understanding of mechanisms and parameters involved in the adaptation process. Because 'stress shielding' is a major issue in long-term integrity of total hip replacements in the next simulation series we created a simple model of stress shielding around a prosthesis and investigated effect of changing bone cells related parameters. We also performed a comparison of this model and a topology optimization scheme. Surprisingly both procedures produced very similar results. Apparently this bone adaptation model has qualities similar to those of global optimization.**

INTRODUCTION

Bone cells come into existence with the genetic blueprint for skeleton and sculpt it during growth until the skeletal design meets the loading demands. This process, termed *bone adaptation*, requires bone cells to detect mechanical signals and integrate these signals into proper changes in the bone architecture. Specialized cells, osteoclasts and osteoblasts, respectively are in charge of bone resorption and formation.

Although mechanisms involved in the regulation of these 'actor' cells are still vague, it is evident that mechanical feedback must be involved ([1]; [2]).

By closely following the latest developments in bone physiology, many researchers have tried to develop mathematical models for the bone adaptation process. In 1976, Cowin and Hegedus [3] developed a sophisticated continuum, thermo-mechanical theory so-called adaptive elasticity theory. In this model, bone is defined as a porous medium with two phases: an elastic structure and an extracellular fluid. According to this model, adaptation is controlled by strain. Following adaptive elasticity theory, many other theories have been developed by others. For example, Rouhi et al. [4] replaced volume fraction by free surface density in the constitutive equations; Also Rouhi et al. [5] added a microcrack factor in the remodeling equations; Huiskes et al. [6] suggested that instead of strain, strain energy density (SED) can be used as a suitable mechanical stimulus for remodeling.

In the beginning of the 21st century, Huiskes and co-workers [7] developed a more refined semi-mechanistic theory. The new theory was based on the regulation scheme depicted in Figure 1. The purpose of this research is to simulate this model by developing a MATLAB code as the framework for further investigation of its capabilities and to have a better insight into adaptation of bone predicted by this model. In addition, effects of the parameter values in the model, Finite Element mesh and the external load and loading direction on the predicted morphology will be studied. Also two other simulation series including stress shielding simulation and a comparison with a topology optimization code will be performed.

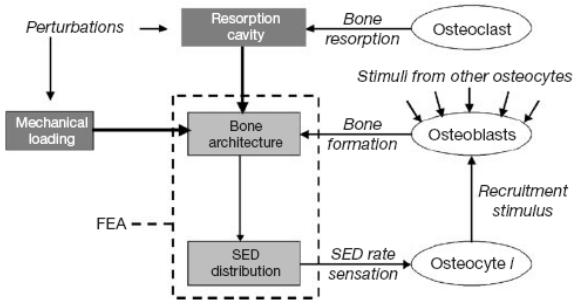

Fig.1. The regulatory process proposed by Huiskes and co-workers [7].

METHODS

In computational model presented by Huiskes et al. [7] bone tissue is assumed to contain n osteocyte cells per cubic millimeters located in the mineralized matrix with a total of N in the domain considered.

Each osteocyte i measures a mechanical signal $R(t)$ (in $\mathrm{J\,m^{-3}s^{-1}}$), the strain energy density (rate), in its location. In turn the osteocyte recruits osteoblasts to form new bone depending on the difference between the measured signal

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and a reference signal, *k*. The influence of an osteocyte on its environment is assumed to decrease exponentially with increasing distance from the osteoblasts. The influence of osteocytes *i* on the osteoblast at location *x* is described by the spatial influence function

$$f_i(x) = exp(-d_i(x)/D), \quad (1)$$

where $d_i(x)$ is the distance between osteocyte *i* and location *x*. The parameter *D* represents the distance from an osteocyte at which location its effect has reduced to e^{-1}; i.e. 36.8% [8].

The osteoblast recruitment stimulus is given by the stimulus value *P(x,t)* to which all osteocytes contribute relative to their distance from x, hence

$$P(x,t) = \sum_{I}^{N} f_i(x)\mu_i R_i(t) \quad (2)$$

where μ_i is mechanosensitivity of osteocyte *i*.

The regulation of the relative density m in location *x* is governed by

$$\frac{dm}{dt} = \tau\{P(x,t) - k\} - r_{oc} \quad \text{for } P(x,t) > k$$

$$\frac{dm}{dt} = -r_{oc} \quad \text{for } P(x,t) \le k \quad (3)$$

where τ is a constant regulating the rate of the process, *k* is the threshold level for bone formation and r_{oc} is the relative amount of mineral resorbed by osteoclasts per day [7] .

This model includes a probability *p* of osteoclast activation per surface site at any time. This probability is assumed to be regulated either by the presence of microcracks or by disuse. The probability of resorption by microcracks was considered spatially random and was expressed as

$$p(x,t) = \text{constant}, \quad (4)$$

where this constant was selected to be 10%. When assuming osteoclastic activation by disuse, the probability of resorption is higher in areas of lower strain. This strain dependent probability was formulated as

$$p(x,t) = c[a - P(x,t)] \quad \text{if } P < a$$

$$p(x,t) = 0 \quad \text{if } P \ge a \quad (5)$$

where *c*=12.5 and *a*=1.6 [7].

The elastic modulus *E*(*x,t*) at each location is calculated from density according to ([8])

$$E(x,t) = b \times m(x,t)^{\gamma} \quad (6)$$

where *b* and γ are constants.

Simulations were performed on a $2 \times 2 \ mm^2$, two dimensional bone FE model. The structure was loaded by distributed stresses of 2 *MPa* at the edges and frequency of the load was sinusoidal at 1Hz [7].

We created the two-dimensional model by implementing above mathematical expressions in combination with FE formulation in a MATLAB code.

The plate was meshed with 40x40 and 80x80 (only for the first simulation) four-node bilinear quadrilateral elements (Fig. 2). The sensor distribution was uniform associated with a sensor influence parameter of *D* = 0.01 *mm* and sensor density was assumed to be 1600/mm^2 [8]. In

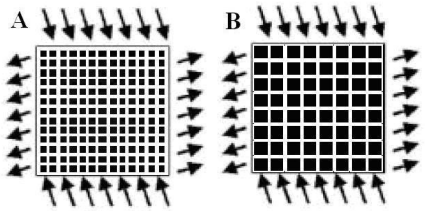

Fig.2. Initial configuration (post-mineralized fetal stage) for (A) 40x40 and (B) 80x80 element models.

all simulations we only considered case of spatial random resorption with a probability of 10% because as stated by Huiskes et al [7] the only effect of strain-regulated resorption, is in the kinetics of the process. The homeostatic architecture is maintained but develops much faster in the simulation [7]. It means these two conditions are equivalent in the theory.

The computations were performed on a Pentium 3 GHz CPU with 1 MB of RAM.

RESULTS

Ten different simulations were performed. The first and second ones tested whether the theory produces trabecular-like 2D configurations from conceptual initial architectures, representing bone in the post-mineralized fetal stage and from a uniform density (Fig. 3). Simulations were prolonged until no more gross architectural changes occurred, representing the homeostatic mature stage.

In these two simulations the structures remodeled toward similar homeostatic configurations, in which trabecular-like structures were created and trabeculae were aligned to the loading direction (Fig. 3). Increasing the number of elements produced the same results.

In the third simulation when the external load applied to the homeostatic architecture was rotated by 25°, the orientation of the trabeculae gradually reorientated as well, to align again with the external load (Fig. 4).

In the forth simulation the regulatory mechanism was able to adapt the structure to alternative loading conditions. A 25% increase in loads produced increased trabecular thickness and gain of bone mass (Fig. 5).

The effect of overloading and unloading on trabecular adaptation was investigated in the fifth simulation where we artificially disconnected two trabeculae while the same externally applied load was maintained. The disconnected and therefore unloaded tarbeculae disappeared, while the neighboring overloaded trabeculae thickened (Fig. 6).

In the sixth simulation by increasing Young's modulus for the upper side of square plate a simple model of stress-shielding of bone around prosthesis was simulated. Bone resorption happened close to the implant surface and this continued until a new homeostasis was obtained (Fig. 7).

In the seventh, eighth and ninth simulations we changed bone resorption and formation related parameters. Decreasing r_{oc} and $p(x,t)$ by 50% had similar effects on bone loss due to stress shielding (Fig. 8 A, B). In both cases the severity of bone loss was reduced and trabeculae close to the implant were thickened. But in case of increasing

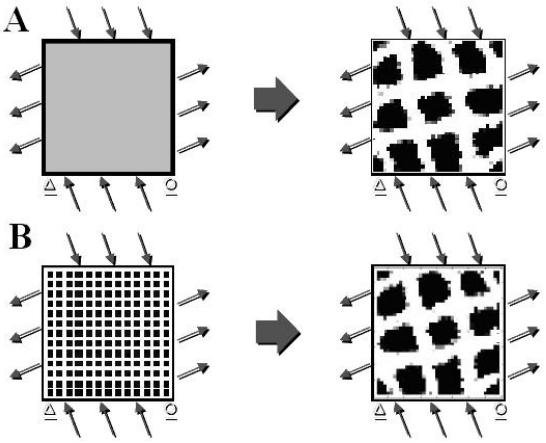

Fig.3. Transformation of morphology for (A) uniform density (B) post-mineralized fetal stage initial configurations

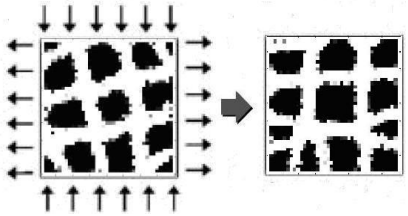

Fig.4. Orientation of the applied stresses was changed from 15° to 0° and the architecture adapted to align with the new stress orientation.

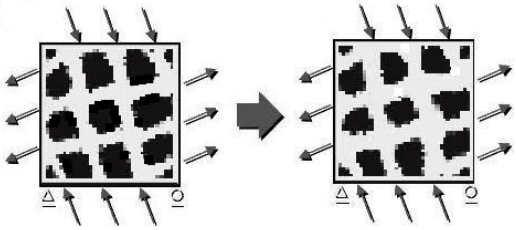

Fig.5. Effect of increasing loading magnitude by 25%. All trabeculae thicken.

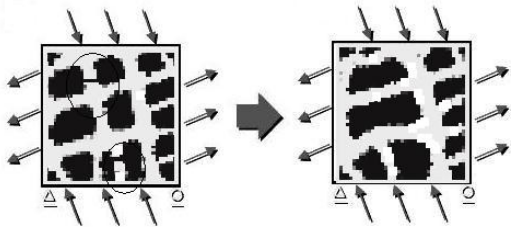

FIG.6. Two struts are artificially disconnected, while the external stress is maintained. After adaptation, the existing architecture is again adapted to the applied stresses by removal of the unloaded trabeculae and thickening of the overloaded trabeculae.

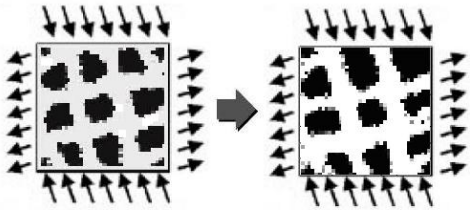

FIG. 7. Stress shielding is simulated by increasing the young modulus of upper side of the square.

bone formation rate by 50% the change in rate of bone loss was little (Fig. 8 C). A trabecula in top right corner of the first two models was maintained but in the bone formation enhanced model this trabecula disappeared.

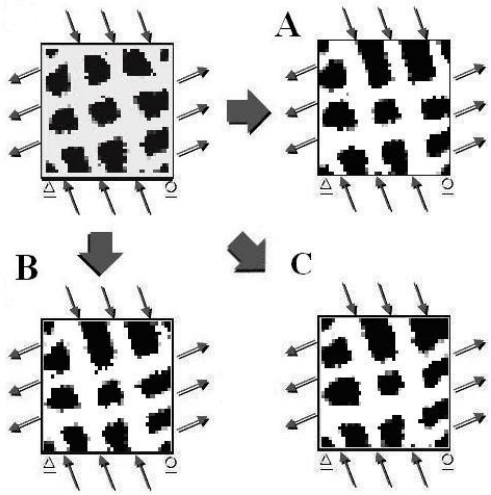

FIG.8. Effect of stress shielding coupled with (A) Decreasing r_{oc} by 50% (B) Decreasing $p(x,t)$ by 50% and (C) increasing bone formation rate by 50%.

In the tenth simulation the question was how will this remodeling theory compare to a topology optimization model? We obtained very similar final configurations (Fig. 9) by using our code (bone adaptation theory prediction) and the topology optimization code by ole Sigmund [9].

Although this simulation was performed for a simple loading condition (compressive ramp load) but the similarity between the two final configurations is interesting.

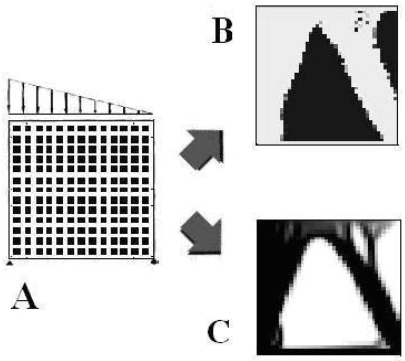

Fig.9. (A) Two-dimensional plate model of bone tissue subjected to a compressive load as indicated (B) Architecture after applying the bone adaptation theory (C) Architecture after applying the topology optimization code.

DISCUSSION AND CONCLUSION

From first five simulations it was concluded that the theory was able to explain both modeling as well as remodeling of trabecular-like architectures as governed by external forces.

Although we implemented the mathematical model in a computer code from scratch, we obtained final configurations very similar to the ones obtained by Huiskes et al. The differences between the figures shown here and the figures from Huiskes et al. [7] are due to a difference in the time increments and time constant used in the formulation. Osteoblasts and osteoclasts were often assumed to work together in bone. In a recent paper Pogoda et al [10]

discuss that bone resorption is independent of bone formation. Studying transgenic mice, they induced a near-complete and reversible osteoblast ablation. In these animals, osteoblast ablation led to a complete arrest of bone formation accompanied by bone loss, thus illustrating that, in mice, the bone resorption function is independent of bone formation [10]. They also provide clinical evidence that the sympathetic regulation of bone does exist in humans and plays a clinically important role in diseases.

A merit of this theory is that it is not in contrast with these latest findings in bone physiology because in this theory there is still a place for biochemical factors and central control of bone remodeling. This model does not imply that biochemical pathways or central control are irrelevant, but it does show that mechanical feedback can be a potent coupling factor for the relevant biochemical processes to take place [7].

Simulation of stress-shielding was another capability of the theory. A major problem threatening the long-term integrity of total hip replacement is the loss of proximal bone often found around non-cemented stems in the long term [6]. It is generally accepted that 'stress shielding' is the cause for this problem: after implantation of the prosthesis the surrounding bone is partially 'shielded' from load carrying and starts to resorb.

Our simulations also suggest (very qualitatively) that anti-resoptive strategy can be more effective than increasing bone formation in treatment of bone loss around implants.

Another interesting result was that when the global optimization procedure was applied to structures similar to those we used in this research, they produced results that are analogous. The implication is that the trabecular architecture predicted by this bone adaptation model has qualities of global mechanical optimality.

Maybe more complete theories will appear as our knowledge of cellular processes in body progresses which includes the biochemical pathways and central control of bone remodeling. But this only depends on the parallel advancing of many sciences including genetics, biomechanics, biochemistry and computational techniques.

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